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Early visual impairment is independent of the visuocognitive and memory disturbances in Alzheimer's disease

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Abstract

Static and dynamic contrast sensitivity (SCS and DCS), semantic object identification, and verbal recall functions were evaluated in 20 Alzheimer's disease (AD) patients and in 20 control subjects. We found general SCS and DCS loss in the 0.48–14.34 c deg^{-1} spatial frequency range. In relation to the cognitive functions, semantic object identification was intact, whereas explicit memory was markedly impaired in the AD group. There was no significant correlation between the CS and the memory disturbances. The results suggest that early visual impairment and higher-level cognitive disturbances are independent in AD.

Keywords: Alzheimer's disease; Contrast sensitivity; Parallel visual pathways; Memory; Visuocognitive

1. Introduction

Several studies have reported impaired visual contrast sensitivity (CS) in Alzheimer's disease (AD) (for review, see Bodis-Wollner, Tagliati, Peppe & Antal, 1993). However, the results are contradictory. In some cases, a marked CS loss was found at low spatial frequencies (SFs) as opposed to normal aging, which is characterized by high SF disturbances. Cronin-Golomb, Corkin and Rizzo (1991) demonstrated depressed CS at 0.5 and 1 c deg^{-1}, while higher SFs appeared to be spared when a 0.3 Hz temporal modulation was administered. Using a static chart test, AD patients showed a generalized CS deficit in the range of 1.5 to 18 c deg^{-1}. In contrast, Hutton, Morris, Elias and Poston (1993) found CS loss to 4 Hz modulated patterns only above 2 c deg^{-1}. A few studies reported no CS deficit, suggesting that visual deficits are restricted to higher-level functions in AD such as object recognition and complex spatial-visuomotor tasks (Schlotterer, Moscovitch & Carpper-McLachlan, 1983; Wright, Drasdo & Harding, 1987; Hof, Vogt, Bouras & Morrison, 1997). Studies reporting CS deficit to high temporal and low spatial frequencies, hypothesized the specific impairment of magnocellular pathway in AD (Bassi & Lehmkuhle, 1990; Lakshminarayanan, Lagrave, Kean, Dick & Shankle, 1996). Recently, this theory has been challenged from both functional and morphological points of view (Kurylo, Corkin, Dolan, Rizzo, Parker & Growdon, 1994; Leuba & Saini, 1995; Hof et al., 1997). The heterogeneous patient populations and differing methodologies (e.g. using different temporal frequencies) might explain the discrepancies outlined above. Different patterns of neuronal degeneration in the visual system, reflecting the stage of the disease, may lead to different CS losses. Conversely, stimuli differing in spatial and temporal characteristics may stimulate different set of neurons. However, the relationship between early visual dysfunction and higher-level visuocognitive/memory disturbance has not been clarified. The aim of the present study was to gain more information about CS in AD patients with a relatively high functioning and to elucidate the relationship between CS disturbance and cognitive dysfunction.

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2. Methods

2.1. Subjects

A total of 26 patients (16 female and 4 male) who met the DSM III-R (Diagnosis and Statistical Manual of Mental Disorders, American Psychiatric Association, 1987) criteria of senile dementia of Alzheimer type, together with 20 healthy control subjects (16 female and 4 male), participated in the study. The mean age of AD patients was 72.8 years (SD = 5.1), while that of the controls was 73.1 (SD = 7.8). The mean score of the Mini-Mental State Examination (MMSE) was 21.6 (SD = 6.3) (Folstein, Folstein & McHugh, 1975). The mean visual acuity was 6/10.2 (SD = 0.4) in the AD group and 6/9.1 (SD = 0.3) in the control group. In most cases, CT, MRI and SPECT scans were performed. The exclusion criteria included psychosis, depression, drug-abuse, diabetes, hypertension and other neurological/ophthalmological disorders.

2.2. CS measurements

Monocular static and dynamic CSs (SCSs and DCSs, respectively) were measured at nine SFs (0.48, 1.19, 1.91, 2.87, 3.58, 4.78, 5.73, 7.17, and 14.34 c deg^{-1}) with a computerized test (Venus, NeuroScientific Corporation, USA). Stimuli were luminance contrast horizontal gratings with a sinusoidal luminance profile. For the DCS test the pattern was reversed at the rate of 4 Hz. The display subtended a visual angle of $13 \times 13°$ and was viewed from a distance of 1 m. The background luminance was 40 cd m^{-2}. The maximum contrast was 70.7%. We used a method of adjustment. It is known that the two-alternative forced choice staircase is a proper method to measure sensory parameters. However, this is not the case for aged people with declining attention and memory. Pairing gratings with sounds and selecting keys to answer is demanding and exhausting, causing errors that come from attention and memory deficit rather than sensory impairment (e.g. forgetting which key to press). Threshold measurements controlled by the experimenter help to adjust experimental parameters according to the needs of patients and to exclude response bias and attentional fluctuations that may occur in the case uncontrolled response selection.

First, the contrast was set at 15 dB above the mean normal value. Participants were able to detect this submaximal contrast level. The contrast level was decreased by 3 dB every 5 s until subjects were not able to detect the stimulus (descending method). Next, contrast was set at 15 dB below the threshold measured with the descending method. For the ascending method, the contrast was increased by 3 dB every 5 s until subjects detected the stimulus. The whole procedure was repeated five times to obtain a mean contrast threshold at a SF. CS was defined as the reciprocal of the contrast threshold (Robson, 1966). The sequences of the descending and ascending methods, the SFs tested, and the static versus dynamic tests were counterbalanced across subjects.

2.3. Enhanced cued recall test

Semantic object identification and memory functions of AD patients were evaluated with the Enhanced Cued Recall Test (ECRT) (Grober & Buschke, 1987; Grober, Buschke, Crystal, Bang & Dresner, 1988). In the first phase, line drawings of 16 common objects from different semantic categories were presented to the subjects. A category cue was given verbally by the experimenter (e.g. 'fruit'). The participants were requested to point to and name each item of the category (e.g. 'grapes' for category 'fruit'). This was followed by an immediate recall to ensure encoding. The three subsequent recall phases consisted of a free recall and a cued recall test. Firstly, AD patients were asked to remember and name as many items as they could (free recall). Secondly, when the free recall was exhausted the category cue of the unrecalled items was given (cued recall). The performance was expressed as the number of recalled items. Total recall was defined as the sum of items from the free and cued phases (for methodological details, see Grober & Buschke, 1987; Grober et al., 1988).

3. Results

3.1. SCS and DCS functions

A $\log_{10}$ transformation was performed on the raw data. In the statistical analysis, the CSs of both left and right eyes were included in the same analysis of variance (ANOVA). A 2 (group) × 2 (temporal modulation) × 9 (SF) ANOVA revealed significant main effects of group ($F(1,78) = 22.03$; $P < 0.0001$) and SF ($F(8,624) = 841.27$; $P < 0.0001$). There were significant interactions between group and SF ($F(8,624) = 9.80$; $P < 0.0001$) as well as between temporal modulation and SF ($F(8,624) = 30.82$; $P < 0.0001$). In the AD group, the Newman–Keuls test revealed significantly impaired SCS and DCS at each SF ($P < 0.01$) (Fig. 1).

3.2. Interocular comparisons

To compare CSs obtained from the left and right eyes, each eye was included as an independent variable in the group by temporal modulation by SF ANOVA. This ANOVA revealed no main effect of eye or any relevant interaction. In addition, there was a significant correlation between the CS values of the left and right

eyes ($r > 0.6$, $P < 0.01$). These results revealed no significant differences between the CSs of the left and right eyes and demonstrated a parallel CS loss.

3.3. Enhanced cued recall test

In the semantic object identification task, the AD patients were able to find and name the cued items. The average numbers of recalled items in the three phases were 3.8 (free)/6.2 (total) (SD = 1.7/2.1), 3.2 (free)/7.8 (total) (SD = 0.9/3.5), and 3.5 (free)/7.7 (total) (SD = 2.1/1.9), respectively.

3.4. Relationship between early visual impairment and cognitive deficits

To evaluate the possible association between early visual impairment and cognitive disturbances, correlation coefficients were calculated for the SCS/DCS values and the MMSE/ECRT scores. There was no significant correlation between the CS values and the MMSE scores ($r < 0.3$). The CS also appeared to be independent of the memory functions assessed with the ECRT ($r < 0.4$ for the free, cued, and total recall scores from the three test phases). The results were similar when the MMSE/ECRT scores were included as covariants in the group by temporal modulation by SF ANOVA.

4. Discussion

The results of this study can be summarized as follows: (1) AD patients had CS deficits in the range of SF tested. (2) There was an interocular correlation of CS deficit, although this effect was not robust. (3) Semantic object identification was spared, suggesting relatively intact visuocognitive and lexical functions. (4) There was a severe explicit memory impairment in the AD group. The ECRT results were consistent with the findings of previous studies (Grober & Buschke, 1987 and Grober et al., 1988). (5) The CS impairment showed no correlation with the MMSE/ECRT scores.

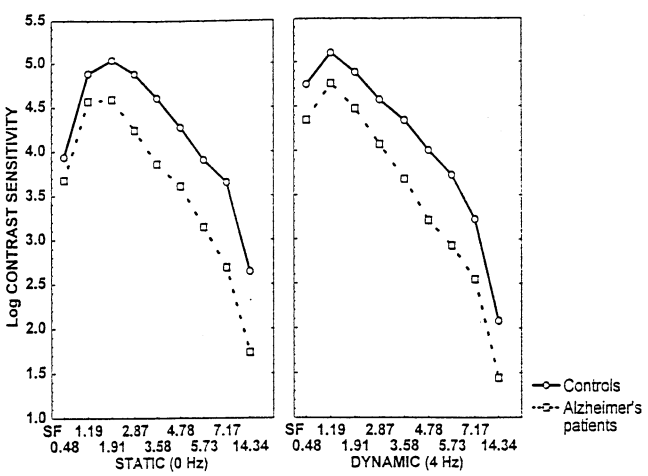

Fig. 1. The figure illustrates static and dynamic contrast sensitivities of control subjects and Alzheimer's disease patients. There were no interocular differences (Section 3) hence these curves represent mean values from both eyes. Spatial frequency (SF) (cycles/degree (c deg^{-1})) is represented on the horizontal axis.

The present study found a generalized CS loss in both static and dynamic conditions. This is consistent with the study of Gilmore and Levy (1991) which revealed a general CS deficit at low, medium, and high SFs. It is interesting to speculate about the neuronal mechanisms of CS impairment in AD. In the primate visual cortex, there are low spatial frequency-sensitive regions, called blobs. Blobs are rich in cytochrome oxidase (CO) activity. Conversely, CO-poor interblobs are sensitive to high spatial frequency stimuli (Tootell, Silverman, Hamilton, Switkes & DeValois, 1988). The functional characteristics of these cortical structures may be related to the precortical magno- and parvocellular pathways (Bassi & Lehmkuhle, 1990). In relation to the cortical origin of low SF loss, one can hypothesize that CO-rich blobs of the striate cortical layers II-III are impaired. These high-energy demand cells may be especially vulnerable because of the dysfunction of terminal oxidative mechanisms in AD (Tootell et al., 1988; Bassi & Lehmkuhle, 1990; Blass & Gibson, 1991; Zeevalk & Nicklas, 1991; Wong-Riley, Antuono, Ho, Egan, Hevner, Liebl, Huang, Rachel & Jones, 1997). However, there are several limitations of this hypothesis. (i) Although CO-rich blobs can exhibit a prominent vulnerability, it is unlikely that they are selectively afferented by the magnocellular pathway (for review, see Bassi & Lehmkuhle, 1990). (ii) Layer IVC-beta (receiving parvocellular afferents) has greater CO activity than IVC-alpha (receiving magnocellular afferents) in the adult human brain (Wong-Riley, Hevner, Cutlan, Earnest, Egan, Frost & Nguyen, 1993). Thus, in this case the vulnerability of the parvo-recipient structures should be higher. (iii) The pattern of amyloid angiopathy suggests that the whole layer IV is affected in AD, including layer IVB, which is believed to be the first converging site of the magno- and parvocellular pathways (Sawatari & Callaway, 1996; Kuljis & Tikoo, 1997). However, the visual deficits arising as the result of amyloid angiopathy are unknown. Kuljis and Tikoo (1997) reported that senile plaques are relatively infrequent in layer IV of the striate cortex, while Beach and McGeer (1992) found strong laminar amyloid immunoreactivity in the layer IVC. The relationship between amyloid deposits/angiopathy and oxidative failure is also unclear. (iv) A recent study demonstrated that both blobs and interblobs exhibit reduced CO activity in AD. However, the individual variability is high, and the activity may depend on the severity and

length of the illness (Wong-Riley et al., 1997). Therefore, our results suggest that the visual system deficits of AD patients are not restricted to the magnocellular pathway and its cortical projection sites. The significant interocular correlation may suggest a cortical origin of CS impairment, although a parallel degeneration of the optic nerves is possible (Hinton, Sadun, Blanks & Miller, 1986).

The impairment of semantic memory and visual object recognition is common in AD (Bayles & Kaszniak, 1987; Mendez, Mendez, Martin, Smyth & Whitehouse, 1990; Hof & Bouras, 1991; Chan, Butters, Paulsen, Salmon, Swenson & Maloney, 1993; Laatu, Portin, Revonsuo, Tuisku & Rinne, 1997). However, our patients did not show such deficits in the current paradigm used. This is consistent with their relatively high MMSE scores. They were able to recognize and name line drawings of semantic category exemplars on the basis of verbal cues (e.g. 'fruit' for 'grapes'). This task involved both visual and lexical processes. The recognition of living instances is dominantly mediated by the occipito-temporal visual cortex, while for man-made tools cortical areas associated with the functional aspects of objects play a more important role (Martin, Wiggs, Ungerleider & Haxby, 1996).

AD patients in this study had severe explicit memory and early visual (CS) dysfunction, whereas their object recognition and semantic abilities were relatively spared. Although Cronin-Golomb et al. (1991) demonstrated correlation between CS loss and scores of a dementia scale in nine patients, in our study the degree of cognitive dysfunction, as indexed by the MMSE/ECRT scores, did not correlate with the CS loss. Nevertheless, the independence of low-level visual and cognitive disturbances in AD requires further investigation.

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